

REMARKS

This application has been carefully reviewed in light of the Office Action mailed February 14, 2007. Claims 1-34 are pending and stand rejected by the Examiner. Applicants amend Claim 11 for informalities. Reconsideration and allowance of Claims 1-34 is respectfully requested in view of the following remarks.

Procedural History

The non-final Office Action is the fifth action on the merits for this application. The prior art rejections in each of the first four Office Actions were withdrawn without amendment to the claims, but in response to Applicants noting they were incorrect. Applicants now address a fifth Office Action. The reasoning of this fifth Office Action is somewhat sparse, just as with the four previously withdrawn rejections.

Applicants remind the Patent Office of the direction of the M.P.E.P to Supervisory Patent Examiners to impress their Assistants with the fact that the shortest path to the final disposition of an application is by finding the best references on the first search and carefully applying them. *See* M.P.E.P. § 707.02. The Supervisory Patent Examiners are expected to personally check on the pendency of every application which is up for the third or subsequent Office Action with a view to finally concluding its prosecution. *Id.* In addition, any application that has been pending five years should be considered "special" by the Examiner and carefully studied by the Supervisory Patent Examiner. *Id.* In short, every effort should be made to terminate its prosecution. *Id.*

Applicants note that not only is this the fifth Office Action, but that this application has been pending for more than five years, and thus respectfully request the Supervisory Patent Examiner to address this application with a view to terminate its prosecution. Applicants appreciate the time already dedicated by the Supervisory Patent Examiner and Examiner Roy to this end, including the interview with both conducted on March 29, 2007.

Claim Amendment

Claim 11 is amended for informalities. Favorable action is requested.

Double Patenting

Claims 1-34 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-7, 15-40, and 42-47 of U.S. Patent No. 5,865,754 to Sevick-Muraca et al. (“*Sevick-Muraca*”). Applicants respectfully traverse these rejections at least for reasons analogous to Applicants’ response filed January 12, 2004 (“*First Response*”), in which Applicants responded to rejections of the claims based on the same reference. Pages 11 through 13 of the *First Response* described in detail why the entire reference failed to anticipate the claims. In particular, Applicants argued that *Sevick-Muraca* does not teach “selecting a fluorescent contrast agent as a function of a predetermined time-of-flight for a tissue to be imaged in accordance with a mathematical expression modeling the behavior of multiply scattered light traveling through the tissue, the fluorescent,” as recited in Claim 11. Indeed, Applicants noted in the *First Response* that the Office Action mailed September 12, 2003, asserts that this limitation is not shown in *Sevick-Muraca*. See Office Action mailed September 12, 2003, page 5. Applicants note that the rejection was withdrawn as a result of the *First Response*. The double-patenting rejection, therefore, is improper at least because the invention as claimed is not obvious over the entire *Sevick-Muraca* reference and thus not obvious over the *Sevick-Muraca* claims.

During the interview on March 29, 2007, the Examiner mentioned that she had not yet had the opportunity to read the *First Response*, nor the corresponding Office Action. For the convenience of the Examiner, Applicants attach the response filed January 12, 2004 (“*First Response*”). Favorable action is requested.

Section 102 Rejections

The Office Action rejects Claims 1-34 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,321,111 to Perelman et al. (“*Perelman I*”) and U.S. Patent No. 6,070583 to Perelman et al. (“*Perelman II*”). Applicants respectfully traverse these rejections for at least the reasons discussed below.

Claim 1 is allowable at least because the cited references fail to disclose, teach, or suggest “introducing an exogenous fluorescent agent into a biologic tissue, the tissue multiply scattering light with a mean time-of-flight, and the agent having a fluorescence lifetime within a factor of about ten of the mean time-of-flight.” The Office Action relies on identical paragraphs from *Perelman I* (col. 6 lines 61-67, col. 7 lines 1-23) and *Perelman II* (col. 5 lines 13-42) to teach portions of this limitation, but is incorrect in its rejection. More

specifically, the Office Action does not even allege that the cited references disclose “the tissue multiply scattering light with a mean time-of-flight” and “an agent having a fluorescence lifetime within a factor of about ten of the mean time-of-flight.” Applicants respectfully request the Examiner refer to the analogy to the science and mathematics behind a relationship between the time-of-flight and the fluorescent life times provided in the *First Response* on pages 10 through 11. *See* attached.

The Office Action asserts that the references teach “using fluorescence to provide time-of-flight signals with fluorescence lifetimes . . . within a factor of ten of the predetermined time-of-flight.” The cited paragraphs, however, do not even contain “the predetermined time-of-flight” language, nor does such language teach the limitations of Claim 1. In contrast, the paragraphs cited in the Office Action merely disclose experimental results obtained using “time-resolved signals emitted from dye cells embedded in a **polystyrene bead suspension**” (*Perelman I* col. 6 lines 65-66), which does not disclose, teach, or suggest anything about “**tissue** having multiply scattering light with a mean time-of-flight,” as recited in Claim 1. It follows, therefore, that the cited references fail to disclose, teach, or suggest a contrast agent “having a fluorescence lifetime within a factor of about ten of the mean time-of-flight.” The fact that *Perelman I* and *Perelman II* fail to disclose “an agent having a fluorescence lifetime within a factor of about ten of the mean time-of-flight” is confirmed by their summaries, in which they explicitly state that the disclosed “measuring and analyzing . . . is not sensitive to fluorescence lifetime” (*Perelman I* col. 2 lines 23-27; *Perelman II* col. 1 lines 57-60).

However, during the interview on March 29, 2007, the Examiner identified two additional sections of *Perelman I* that the Examiner asserted teaches the above limitations of Claim 1. In particular, the Examiner identified col. 7 lines 1-23, and col. 8 lines 20-45. Even though not addressed in the Office Action, Applicants traverse this assertion for the following reasons. In column 7, *Perelman I* merely compares fluorescence lifetimes of RB and R6G and states “the time-of-flight for these earliest arriving photons is proportional to the depth of the fluorescent object,” which does not disclose, teach, or suggest “introducing an exogenous fluorescent agent into a biologic tissue, the tissue multiply scattering light with a mean time-of-flight, and the agent having a fluorescence lifetime within a factor of about ten of the mean time-of-flight.” In column 8, *Perelman I* states that “[t]hese measurements establish that the early portion of the signal rises rapidly and **is not sensitive to the**

relatively long fluorescence decay time” (col. 8 lines 27-30), which fails to disclose, teach, or suggest the above limitations for reasons already explained.

Claim 1 is allowable also at least because the cited references fail to disclose that a contrast agent is “selected in accordance with a predetermined relationship between degree of contrast and at least one of fluorescence yield or fluorescence lifetime.” The Office Action fails to identify any portion of the cited references that it contends meets this limitation. There is none. In contrast, the references disclose analyzing a signal which “is not sensitive to fluorescence lifetime” (*Perelman I* col. 2 lines 23-27; col. 8 lines 27-30; *Perelman II* col. 1 lines 57-60) and therefore fail to disclose, teach, or suggest, that a contrast agent is “selected in accordance with a predetermined relationship between degree of contrast” and “fluorescence lifetime,” as recited in Claim 1. In addition, the terms “fluorescence yield” do not appear in either cited references.

During the interview on March 29, 2007, the Examiner asserted that column 1, line 62, through column 2, line 35, of *Perelman I* teaches the latter mentioned limitations of Claim 1. Although not addressed in the Office Action, Applicants respectfully traverse such an assertion at least because this section of *Perelman I* fails to even mention the terms “fluorescence yield.” In addition, as previously mentioned, this section describes “measuring and analyzing the early portion of the fluorescence signal . . . , which rises rapidly and is not sensitive to fluorescence lifetime.” This section, therefore, fails to disclose that a contrast agent is “selected in accordance with a predetermined relationship between degree of contrast and at least one of fluorescence yield or fluorescence lifetime.”

For at least the above reasons, Claim 1 is allowable, as are all claims depending therefrom. Favorable action is requested.

Independent Claims 11 and 17 are allowable at least for analogous reasons. In particular, the cited references fail to disclose, teach, or suggest “the fluorescent contrast agent having a fluorescence lifetime within a factor of ten of the predetermined time-of-flight,” as recited in Claim 11, as amended. Regarding Claim 17, the cited references fail to disclose, teach, or suggest “evaluating ability of a number of fluorescent agents to provide image contrast between different tissue types, said evaluating including determining a relationship between degree of image contrast and at least one of fluorescence lifetime or fluorescence yield of the agent.” For at least these reasons, independent Claims 11 and 17 are allowable, as are all claims depending therefrom. Favorable action is requested.

Claim 23 is allowable at least because the cited references fail to disclose, teach, or suggest “exposing a biologic tissue to a first excitation light; detecting a first emission from the tissue in response to the first excitation light; introducing a fluorescent contrast agent into the tissue after said detecting; exposing the tissue after said introducing to a second excitation light” and “sensing a second emission in response to the second excitation light.” The Office Action incorrectly asserts that the cited references disclose “exposing a biological tissue to first and second excitation light and detecting first and second emission [sic] from tissue in response to the excitation light” and “introducing an exogenous fluorescent contrast agent into the tissue after detecting.” The Office Action mischaracterizes four sections of each cited reference in an attempt to support this assertion.

The first section cited by the Office Action merely provides an overview of a respective device that can deliver excitation light to a sample (*Perelman I* col. 4, lines 59-60; *Perelman II* col. 3, lines 13-34). The second section discloses that the “geometry is applicable to many human organs” (*Perelman I* col. 5, lines 61-67; *Perelman II* col. 4, lines 22-28). The third section merely “illustrates the use of a fiberoptic probe in determining the location of the fluorescent object in three dimensions by observing the time-resolved fluorescent signal” (*Perelman I* col. 6, lines 56-59; *Perelman II* col. 5, lines 8-11). The fourth section merely suggests the use of dyes (*Perelman I* col. 8, lines 57 through col. 9 line 7; *Perelman II* col. 7, lines 16-32). If it were even appropriate to combine each of these separate sections into a single context, which Applicants respectfully traverse, even collectively the sections fail to disclose, teach, or suggest the above limitation at least because they fail to disclose “exposing a biologic tissue to a first excitation light” and “exposing the tissue after said introducing to a second excitation light.” Moreover, even if the Office Action assertion was valid, which clearly it is not, merely “introducing an exogenous fluorescent contrast agent into the tissue after detecting” fails to disclose, teach, or suggest “exposing the tissue **after** said introducing,” as recited in Claim 23.

In addition, Claim 23 is allowable at least because the cited references fail to disclose, teach, or suggest “comparing data corresponding to the first emission with data corresponding to the second emission to evaluate contrast provided by the agent as a function of at least one of fluorescence lifetime, fluorescence yield, or quantum efficiency.” The Office Action relies on similar paragraphs from *Perelman I* (col. 6 lines 52-60) and *Perelman II* (col. 5 lines 13-25) to teach this limitation, but this is incorrect. The cited paragraphs merely disclose timing photon migration emitted from fluorescing material or lesions A, B,

and C, which does not constitute “comparing data corresponding to the first emission with data corresponding to the second emission to evaluate contrast provided by the agent as a function of at least one of fluorescence lifetime, fluorescence yield, or quantum efficiency.”

For at least these reasons, Claim 23 is allowable, as are all claims depending therefrom. Favorable action is requested.

Applicants note that, in the very least, the Office Action fails to directly address the rejections of dependent Claims 2, 7, 9, 18, 24, and 31. Favorable action is requested.

Conclusion

Applicants have now made an earnest attempt to place this case in condition for immediate allowance. For the foregoing reasons and for other apparent reasons, Applicants respectfully request allowance of all pending claims.

If the Examiner feels that prosecution of the present Application may be advanced in any way by a telephone conference, the Examiner is invited to contact the undersigned attorney at 214-953-6447.

Applicants do not believe that any fees are due. However, the Commissioner is hereby authorized to charge any fees or credit any overpayments to Deposit Account No. 02-0384 of Baker Botts L.L.P.

Respectfully submitted,

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